



Appendix A

Claim Amendments

1-20. (Canceled)

21. (New) A method of treatment or prophylaxis of a disease associated with or based on impairment or dysfunction of cerebral vascular reactivity selected from the group consisting of sepsis associated encephalopathy, sepsis, toxic encephalopathy, encephalopathy associated with autoimmune thyroiditis, autoimmune thyroiditis, cerebral microangiopathy, hypercholesterolemia and hypertriglyceridemia in a patient afflicted with such disease comprising the step of administering a pharmacologically tolerable and therapeutically effective amount of a PDE5 inhibitor to the patient.

22. (New) The method according to claim 21, wherein the disease is sepsis associated encephalopathy.

23. (New) The method according to claim 21, wherein the PDE5 inhibitor is selected from the group consisting of 3-

ethyl-8-[2-(4-morpholinylmethyl)benzylamino]-2,3-dihydro-1H-imidazo[4,5-g]quinazoline-2-thione, 1-(2-chlorobenzyl)-3-isobutyryl-2-propylindole-6-carboxamide, 9-bromo-2-(3-hydroxypropoxy)-5-(3-pyridylmethyl)-4H-pyrido[3,2,1-jk]-carbazol-4-one, 4-(1,3-benzodioxol-5-ylmethylamino)-2-(1-imidazolyl)-6-methylthieno[2,3-d]pyrimidine, 6-(2-isopropyl-4,5,6,7-terahydropyrazolo[1,5-a]pyridin-3-yl)-5-methyl)-5-methyl-2,3,4,5-tetrahydropyridazin-3-one, 5-(4-methylbenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 3-(1-methyl-4-phenylbutyl)-5-pyridin-4-ylmethyl-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(4-bromobenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-benzyl-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(3,4-dimethoxybenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(3,4-dichlorobenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-biphenyl-4-ylmethyl-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(4-aminobenzyl)-3-(1-methyl-4-

phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(hydroxyphenylmethyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo-[4,5-d]pyrimidin-7-one, 5-benzo[1,3]dioxol-5-ylmethyl-3-[1-methyl-4-phenylbutyl]-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, N-4-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]triazolo-[4,5-d]pyrimidin-5-ylmethyl]phenylacetamide, 5-benzoyl-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 3-(1-methyl-4-phenylbutyl)-5-[4-(morpholine-4-sulphonyl)benzyl]-3,6-dihydro[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 3-(1-methyl-4-phenylbutyl)-5-[3-(morpholine-4-sulphonyl)benzyl]-3,6-dihydro[1,2,3]triazolo[4,5-d]pyrimidin-7-one, N-methyl-4-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]-triazolo-[4,5-d]pyrimidin-5-ylmethyl]-benzenesulphonamide, N-(2-dimethylaminoethyl)-4-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-ylmethyl]benzenesulphonamide, N-(2-hydroxyethyl)-4-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-ylmethyl]benzenesulphonamide, ethyl 1-[3-[3-(1-methyl-4-

phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]-triazolo-
[4,5-d]pyrimidin-5-
ylmethyl]benzenesulphonyl]piperidinecarboxylate, 3-(1-
methyl-4-phenylbutyl)-5-[4-(4-methylpiperazin-1-
sulphonyl)benzyl]-3,6-dihydro-[1,2,3]triazolo[4,5-
d]pyrimidin-7-one, 5-benzo[1,3]dioxol-5-ylmethyl-3-[1-
ethy-heptyl]-3,6-dihydro-[1,2,3]-triazolo[4,5-
d]pyrimidin-7-one, 3-[1-(1-hydroxyethyl)-4-phenylbutyl]-
5-[4-(morpholine-4-sulphonyl)benzyl]-3,6-dihydro-
[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-[6-fluoro-1-
(phenylmethyl)-1H-indazol-3-yl]-2-furanmethanol, 1-
benzyl-6-fluoro-3-[5-(hydroxymethyl)furan-2-yl]-1H-
indazole, 2-(1H-imidazol-1-yl)-6-methoxy-4-(2-
methoxyethylamino)quinazoline, 1-[[3-(7,8-dihydro-8-oxo-
1H-imidazo[4,5-g]quinazolin-6-yl)-4-
propoxyphenyl]sulphonyl]-4-methylpiperazine, 4-(3-
chloro-4-methoxybenzylamino)-1-(4-hydroxypiperidin-1-
yl)phthalazine-6-carbonitrile, 1-[6-chloro-4-(3,4-
methylenedioxybenzylamino)quinazolin-2-yl]piperidin-4-
carboxylic acid, (6R,12aR)-6-(1,3-benzodioxol-5-yl)-2-
methyl-1,2,3,4,6,7,12,12a-octa-
hydropyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione
(tadalafil), (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-

methyl-6-(3,4-methylenedioxyphenyl)-pyrazino-
[2',1':6,1]pyrido[3,4-b]indole-1,4-dione, 4-ethoxy-2-
phenylcycloheptylimidazole, (6-bromo-3-
methoxymethylimidazo[1,2-a]pyrazin-8-yl)methylamine, 8-
[(phenylmethyl)thio]-4-(1-morpholinyl)-2-(1-
piperazinyl)pyrimidino[4,5-d]pyrimidine, (+)-cis-5-
methyl-2-[4-(trifluoromethyl)benzyl]-3,4,5,6a,7,8,9-
octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one, cis-2-
hexyl-5-methyl-3,4,5,6a,7,8,9,9a-
octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one, 5-[2-
ethoxy-5-(4-methyl-1-piperazinylsulfonyl)phenyl]-1-
methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-
d]pyrimidin-7-one (sildenafil), 1-[[3-(6,7-dihydro-1-
methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-
4-ethoxyphenyl]sulfonyl]-4-methylpiperazine, 2-(2-
propoxyphenyl)purin-6(1H)-one, 2-(2-propoxyphenyl)-1,7-
dihydro-5H-purin-6-one, methyl 2-(2-methylpyridin-4-
ylmethyl)-1-oxo-8-(2-pyrimidinylmethoxy)-4-(3,4,5-
trimethoxyphenyl)-1,2-dihydro-[2,7]naphthyridin-3-
carboxylate, methyl 2-(4-aminophenyl)-1-oxo-7-(2-
pyridinylmethoxy)-4-(3,4,5-trimethoxyphenyl)-1,2-
dihydroisoquinoline-3-carboxylate, 2-[2-ethoxy-5-(4-
ethylpiperazin-1-ylsulfonyl)phenyl]-5-methyl-7-

propylimidazo[5,1-f][1,2,4]triazin-4(3H)-one
(vardenafil), 3,4-dihydro-6-[4-(3,4-dimethoxybenzoyl)-1-
piperazinyl]-2(1H)-quinolinone (vesnarinone), 1-
cyclopentyl-3-methyl-6-(4-pyridyl)pyrazolo[3,4-
d]pyrimidin-4(5H)-one, 1-cyclopentyl-6-(3-ethoxy-4-
pyridinyl)-3-ethyl-1,7-dihydro-4H-pyrazolo[3,4-d]-
pyrimidin-4-one, 6-o-propoxyphenyl-8-azapurin-6-one,
3,6-dihydro-5-(o-propoxyphenyl)-7H-v-triazolo[4,5-
d]pyrimidin-7-one and 4-methyl-5-(4-pyridinyl)thiazole-
2-carboxamide and the pharmaceutically acceptable
derivatives of these compounds.

24. (New) The method according to claim 3, wherein the PDE5
inhibitor is selected from the group consisting of
sildenafil, vardenafil, tadalafil, a pharmaceutically
acceptable salt thereof and a solvate of the
pharmaceutically acceptable salt thereof.

25. (New) The method according to claim 4, wherein the PDE5
inhibitor is selected from the group consisting of
sildenafil citrate, vardenafil hydrochloride, the
trihydrate of vardenafil hydrochloride and vardenafil
dihydrochloride.

26. (New) The method according to claim 22, wherein the PDE5 inhibitor is selected from the group consisting of 3-ethyl-8-[2-(4-morpholinylmethyl)benzylamino]-2,3-dihydro-1H-imidazo[4,5-g]quinazoline-2-thione, 1-(2-chlorobenzyl)-3-isobutyryl-2-propylindole-6-carboxamide, 9-bromo-2-(3-hydroxypropoxy)-5-(3-pyridylmethyl)-4H-pyrido[3,2,1-jk]-carbazol-4-one, 4-(1,3-benzodioxol-5-ylmethylamino)-2-(1-imidazolyl)-6-methylthieno[2,3-d]pyrimidine, 6-(2-isopropyl-4,5,6,7-terahydropyrazolo[1,5-a]pyridin-3-yl)-5-methyl)-5-methyl-2,3,4,5-tetrahydropyridazin-3-one, 5-(4-methylbenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 3-(1-methyl-4-phenylbutyl)-5-pyridin-4-ylmethyl-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(4-bromobenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-benzyl-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(3,4-dimethoxybenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo-[4,5-d]pyrimidin-7-one, 5-(3,4-dichlorobenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-

d]pyrimidin-7-one, 5-biphenyl-4-ylmethyl-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(4-aminobenzyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-(hydroxyphenylmethyl)-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo-[4,5-d]pyrimidin-7-one, 5-benzo[1,3]dioxol-5-ylmethyl-3-[1-methyl-4-phenylbutyl]-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, N-4-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]triazolo-[4,5-d]pyrimidin-5-ylmethyl]phenylacetamide, 5-benzoyl-3-(1-methyl-4-phenylbutyl)-3,6-dihydro-[1,2,3]triazolo[4,5-d]-pyrimidin-7-one, 3-(1-methyl-4-phenylbutyl)-5-[4-(morpholine-4-sulphonyl)benzyl]-3,6-dihydro[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 3-(1-methyl-4-phenylbutyl)-5-[3-(morpholine-4-sulphonyl)benzyl]-3,6-dihydro[1,2,3]triazolo[4,5-d]pyrimidin-7-one, N-methyl-4-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]-triazolo-[4,5-d]pyrimidin-5-ylmethyl]-benzenesulphonamide, N-(2-dimethylaminoethyl)-4-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-ylmethyl]benzenesulphonamide, N-(2-hydroxyethyl)-4-[3-

(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-ylmethyl]benzenesulphonamide, ethyl 1-[3-[3-(1-methyl-4-phenylbutyl)-7-oxo-6,7-dihydro-3H-[1,2,3]-triazolo[4,5-d]pyrimidin-5-ylmethyl]benzenesulphonyl]piperidinecarboxylate, 3-(1-methyl-4-phenylbutyl)-5-[4-(4-methylpiperazin-1-sulphonyl)benzyl]-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-benzo[1,3]dioxol-5-ylmethyl-3-[1-ethy-heptyl]-3,6-dihydro-[1,2,3]-triazolo[4,5-d]pyrimidin-7-one, 3-[1-(1-hydroxyethyl)-4-phenylbutyl]-5-[4-(morpholine-4-sulphonyl)benzyl]-3,6-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-7-one, 5-[6-fluoro-1-(phenylmethyl)-1H-indazol-3-yl]-2-furanmethanol, 1-benzyl-6-fluoro-3-[5-(hydroxymethyl)furan-2-yl]-1H-indazole, 2-(1H-imidazol-1-yl)-6-methoxy-4-(2-methoxyethylamino)quinazoline, 1-[[3-(7,8-dihydro-8-oxo-1H-imidazo[4,5-g]quinazolin-6-yl)-4-propoxyphenyl]sulphonyl]-4-methylpiperazine, 4-(3-chloro-4-methoxybenzylamino)-1-(4-hydroxypiperidin-1-yl)phthalazine-6-carbonitrile, 1-[6-chloro-4-(3,4-methylendioxybenzylamino)quinazolin-2-yl]piperidin-4-carboxylic acid, (6R,12aR)-6-(1,3-benzodioxol-5-yl)-2-

methyl-1,2,3,4,6,7,12,12a-octa-
hydropyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione
(tadalafil), (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-
methyl-6-(3,4-methylenedioxyphenyl)-pyrazino-
[2',1':6,1]pyrido[3,4-b]indole-1,4-dione, 4-ethoxy-2-
phenylcycloheptylimidazole, (6-bromo-3-
methoxymethylimidazo[1,2-a]pyrazin-8-yl)methylamine, 8-
[(phenylmethyl)thio]-4-(1-morpholinyl)-2-(1-
piperazinyl)pyrimidino[4,5-d]pyrimidine, (+)-cis-5-
methyl-2-[4-(trifluoromethyl)benzyl]-3,4,5,6a,7,8,9-
octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one, cis-2-
hexyl-5-methyl-3,4,5,6a,7,8,9,9a-
octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one, 5-[2-
ethoxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-
methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-
d]pyrimidin-7-one (sildenafil), 1-[[3-(6,7-dihydro-1-
methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-
4-ethoxyphenyl]sulfonyl]-4-methylpiperazine, 2-(2-
propoxyphenyl)purin-6(1H)-one, 2-(2-propoxyphenyl)-1,7-
dihydro-5H-purin-6-one, methyl 2-(2-methylpyridin-4-
ylmethyl)-1-oxo-8-(2-pyrimidinylmethoxy)-4-(3,4,5-
trimethoxyphenyl)-1,2-dihydro-[2,7]naphthyridin-3-
carboxylate, methyl 2-(4-aminophenyl)-1-oxo-7-(2-

pyridinylmethoxy)-4-(3,4,5-trimethoxyphenyl)-1,2-dihydroisoquinoline-3-carboxylate, 2-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulfonyl)phenyl]-5-methyl-7-propylimidazo[5,1-f][1,2,4]triazin-4(3H)-one (varденаfil), 3,4-dihydro-6-[4-(3,4-dimethoxybenzoyl)-1-piperazinyl]-2(1H)-quinolinone (vesnarinone), 1-cyclopentyl-3-methyl-6-(4-pyridyl)pyrazolo[3,4-d]pyrimidin-4(5H)-one, 1-cyclopentyl-6-(3-ethoxy-4-pyridinyl)-3-ethyl-1,7-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one, 6-o-propoxyphenyl-8-azapurin-6-one, 3,6-dihydro-5-(o-propoxyphenyl)-7H-v-triazolo[4,5-d]pyrimidin-7-one and 4-methyl-5-(4-pyridinyl)thiazole-2-carboxamide and the pharmaceutically acceptable derivatives of these compounds.

27. (New) The method according to claim 26, wherein the PDE5 inhibitor is selected from the group consisting of sildenafil, vardenafil, tadalafil, a pharmaceutically acceptable salt thereof and a solvate of the pharmaceutically acceptable salt thereof.

28. (New) The method according to claim 27, wherein the PDE5 inhibitor is selected from the group consisting of

sildenafil citrate, vardenafil hydrochloride, the trihydrate of vardenafil hydrochloride and vardenafil dihydrochloride.